Embryonic stem cell-based generation of rat models for assessing human cellular therapies

Grant Award Details

Embryonic stem cell-based generation of rat models for assessing human cellular therapies

Grant Type: Tools and Technologies III

Grant Number: RT3-07949

Project Objective: To develop novel rat models for assessing the safety and efficacy of human stem cell grafts. We have generated several gene knockout rats using ESC-based gene-targeting technology. A major strength of the ESC approach is the ability, in conjunction with Cre/loxP technology, to generate rats in which genes are inactivated in specific tissues and/or at specific times. We propose to generate an inducible immunodeficient rat model, an inducible cardiomyocyte ablation rat model of cardiomyopathy, an inducible β-cell ablation rat model of diabetes, and a rat model of amyotrophic lateral sclerosis-frontotemporal dementia. We will use these models to assess the safety and efficacy of human pluripotent stem cell derivatives. We will also develop a plan to disseminate rat models and technologies to the scientific community.

Investigator:

Name:	Qilong Ying
Institution:	University of Southern California
Type:	PI

Disease Focus: Other

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $1,334,160

Status: Active

Progress Reports

Reporting Period: Year 1

View Report

Grant Application Details

Application Title: Embryonic stem cell-based generation of small animal models for assessing human cellular therapies

Public Abstract:	Heart failure, diabetes and neurodegenerative diseases are among the leading causes of death and disability worldwide. These diseases are characterized by the loss of specific cell types and can be treated and potentially cured with stem cell-based therapies. Before human stem cells can be used in clinical trials, however, their safety and efficacy need to be tested in animal models. Currently, immunodeficient small animals are the preferred models. However, it is readily apparent that mouse physiology and behavior is not optimal for studying many human conditions, and this has often led to translation failures. Although larger animal models are useful, they are extraordinarily expensive and, consequently, experimental opportunities and replications are very limited. The rat is widely accepted as more similar to the human in its physiology and therefore superior to the mouse, especially for metabolic, cardiac and neurological studies. We recently developed a technology that allows us to create nearly any type of genetically modified rat. Using this technology, we will develop immunodeficient rats and rat models for heart failure, diabetes and neurodegenerative diseases. We will use these models to assess human cellular therapies. Our project will provide the research community with the tools and technology necessary to overcome the current constraints of mouse models and will serve as a better investigative platform for understanding the progression and treatment of human diseases.
Statement of Benefit to California:	Heart diseases, diabetes and neurodegenerative diseases affect hundreds of thousands of people in California. These diseases can be potentially improved or even cured by cell replacement-based therapies. Using the small animal model embryonic stem cell-based gene-targeting technology that we developed, we will create small animal models for heart failure, diabetes and neurodegenerative diseases. These small animal models can closely mimic human conditions, and are not expensive to produce. We will also create an immunodeficient rat model to facilitate the assessment of human stem cell therapies in a xenotransplant context. The models developed in this project will be extremely valuable to many investigators in California. We anticipate that, based on results generated using these animal models, new cellular therapies could be developed and many patients in California could benefit from these new therapies. We also anticipate that the new technologies, cell lines and animal models developed in this project will result in intellectual properties that will bring tax revenue to California.